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DETAILED DESCRIPTION

[Detailed Description of the Invention]**[0001]**

[Field of the Invention] This invention relates to the breeding hair agent which shows outstanding hair growth promoting actions.

[Description of the Prior Art] Many breeding hair agents are known from the former, and it is used for prevention and the therapy of a psoriasis. As medicinal properties of these breeding hair agent, although vitamins, such as stimulants, such as vasodepressor, such as a sialid extract and vitamin-E acetate, and capsicum tincture, pantothenic acid, and biotin, and also the hormone drug, the anti-inflammatory agent, the germicide, etc. are used, A breeding hair agent which was furthermore excellent in the breeding hair operation is desired.

[Problem(s) to be Solved by the Invention] An object of this invention is to provide the breeding hair agent which shows outstanding hair growth promoting actions.

[0002]

[Means for Solving the Problem] If it is used combining tocotrienol, forskolin, or its derivative, the breeding hair effect will be enhanced notably, and this invention is made based on knowledge that an aforementioned problem is effectively solvable. That is, a breeding hair agent, wherein this invention contains (A) tocotrienol, (B) forskolin, its derivative, or an extract of a root of *Coleus forskohlii* (*Coleus forskohlii*) is provided. A breeding hair agent, wherein this invention uses together at least one sort of compounds chosen from a group which becomes the above (A) and the (B) ingredient from fatty acid and alcohol which have the chain length of (C) odd number, and those derivatives further is provided.

[0003]

[Embodiment of the Invention] As an example of (A) tocotrienol blended with the breeding hair agent of this invention as an active principle, the alpha-tocotrienol, the beta-tocotrienol, the gamma tocotrienol, and delta-tocotrienol can be mentioned, and these kinds or two sorts or

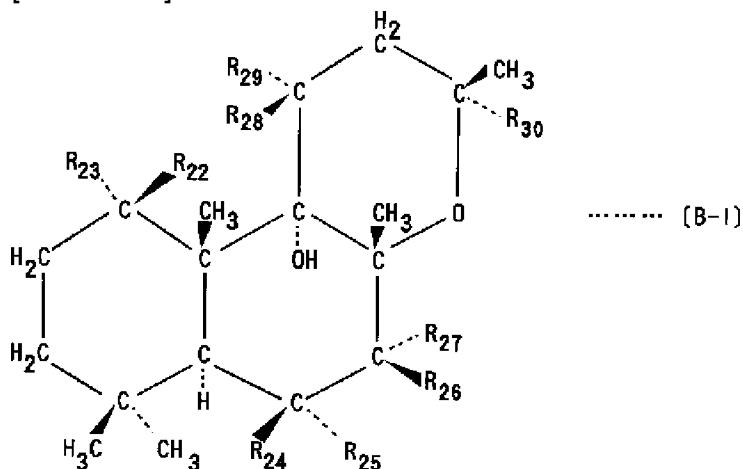
more of mixtures can be used. Although there is an isomer of d-, 1-, and a d1-mold in these tocotrienol, each can be used in this invention. The desirable mode in this invention is a mixture which has a weight ratio of alpha-tocotrienol:gamma-tocotrienol:delta-tocotrienol in the range of A (95:4.8:0.2), B (0.5:99:0.5), C (5:45:50), and D (46:4:50) in a triangular diagram. If the mixture which is within the limits of this is used, the breeding hair effect of having excelled extremely will be revealed.

[0004] Although these tocotrienol is obtained by any methods, such as squeezing of a natural product, extraction from a natural product, and composition, generally it is extracted from the pericarp of the Palmae vegetation, /, and a sowing child. Generally, the tocotrienol obtained from the extract of a natural product is a mixture of two or more tocotrienol. As long as the Palmae vegetation which can be used belongs to Palmae, any may be sufficient, but. *Elaeis guineensis* of the *Elaeis guineensis* group is preferred, and Especially West Africa native *Elaeis guineensis*, *dura*, *pisifera*, and *tenera* which are the hybrid kinds of *Elaeis oleifera* from Central America and *Elaeis odora*, and *Elaeis guineensis* are preferred. Especially the tocotrienol (palm oil tocotrienol) produced by adding water after extraction, and dissociating and chromatography refining has it, and this palm oil tocotrienol, [preferred] Generally it is a mixture of the alpha-tocotrienol, the beta-tocotrienol, the gamma tocotrienol, and delta-tocotrienol. Since the beta-tocotrienol is trace, the presentation of this mixture is usually equivalent to the desirable range said to an above-mentioned triangular diagram.

[0005] The loadings to the breeding hair agent of tocotrienol are 0.01 to 1.0% preferably on the basis of the full weight of a constituent 0.01 to 10.0% of the weight (it is hereafter called % for short). At this invention, it is a following general formula among (B) forskolin and its derivative. It is preferred to use the compound expressed with [B-I].

[0006]

[Formula 1]



[0007] (R₂₂ - R₂₉ among a formula) hydrogen, oxygen, a hydroxyl group, an amino group, and

the carbon numbers 1-25 -- desirable -- the -O-acyl group of 1-19. the carbon numbers 1-25 -- desirable -- the acyl group of 1-19, and the carbon numbers 1-25 -- desirable -- the -O-alkyl group of 1-19. the carbon numbers 1-25 -- it is the alkyl group, diethyl aminomethyl group, or tosyl group of 1-19 preferably, and, in the case of oxygen, a double bond is formed between carbon. Among these, R_{22} or R_{23} , R_{24} , or R_{25} , The thing in which the double bond was formed between carbon is good, without introducing the above-mentioned atom or a basis into the other, when either one of R_{26} or R_{27} , R_{28} or R_{29} is oxygen. The case where oxygen or R_{28} is [R_{29}] hydrogen in a hydroxyl group as R_{28} and R_{29} is more preferred. R_{30} -- hydrogen and the carbon numbers 2-25 -- desirable -- the alkenyl group of 2-19, and the carbon numbers 1-25 -- desirable -- the alkyl group of 1-19, and the carbon numbers 1-25 -- the dialkylamino hydroxyethyl group, aldehyde group, or epoxy group of 1-19 is shown preferably. There may be substituents, such as halogen, in an acyl group and an alkyl group, and the aromatic ring may be included. Carbonate or a sulfonate may be made to form between R_{22} , R_{23} , the hydroxyl group of the 9th place, R_{24} and R_{25} , R_{26} , and R_{27} .

[0008]The above-mentioned general formula In a compound expressed with [B-I], it is forskolin (chemical name: the 7beta-acetoxy 8,13-epoxy- 1alpha and 6beta, 9alpha-trihydroxy rhabdo 14-ene- 11 -). [and] the inside of a formula, R_{22} , R_{25} , and R_{27} -- hydrogen, R_{23} , and R_{24} -- as for an acetoxy group, R_{28} , and R_{29} , in a hydroxyl group and R_{26} , oxygen forms a double bond in either as one-atom ON. A compound, its specific derivative, and those salts of a vinyl group are included for R_{30} . Forskolin used by this invention is the substance by which structure determination was separated, refined and carried out from an extract of a root of Lamiaceae vegetation, such as Coleus forskohlii (Coleus forskohlii), and since it has physiological functions, such as a blood pressure fall operation and muscle contraction power potentiation, it attracts attention these days. It is also possible to obtain from an intermediate besides a method of separating and refining from an extract of a root of the above-mentioned vegetation with a synthetic method as a manufacturing method, and it is already marketed as a biochemistry reagent. It is also possible to use a crude extract of vegetation, such as Coleus forskohlii containing a forskolin related substance, originally extracted with solvents, such as methanol, in this invention, and, Or it is also possible to use what was further separated and refined by methods, such as chromatography, a thing obtained from an intermediate with a synthetic method, or a thing further derivatized with a synthetic method.

[0009]Specifically Forskolin, 14, 15-dihydroforskolin, 11beta-hydroxy forskolin, 1,6-diacetyl forskolin, 7-deacetyl forskolin, 6-acetyl-7-deacetyl forskolin, 7-succinyl 7-deacetyl forskolin, 7-butyryl-7-deacetyl forskolin, 7-tosyl 7-deacetyl forskolin, 6-hexanoyl forskolin, 1-diethylamino methyl-6-acetyl-7-deacetyl forskolin, One sort or two sorts or more of mixtures, such as

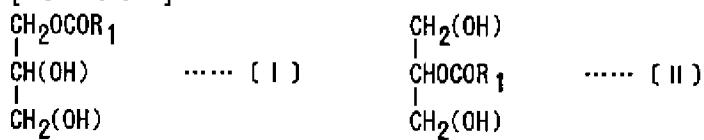
forskolin 1,9-carbonate, a forskolin 1,9-sulfonate, forskolin 6,7-carbonate, and forskolin 1,9;6,7-2 carbonate, are illustrated. Especially a desirable thing is forskolin among the above-mentioned forskolin related substances.

[0010]In this invention, if a compound of an ingredient (A) and a compound of an ingredient (B) are used together and it gives directly scalp, the stronger breeding hair effect demonstrates and a compound of an ingredient (B) can be blended by arbitrary concentration into a breeding hair agent. Usually, it is good to blend 0.0001 to 5% preferably 0.00001 to 10% on the basis of full weight of a breeding hair agent with types of products and frequency in use. Especially a desirable thing is 0.01 to 5%. As a result of searching for a synergistic effect of the above-mentioned structure material blended into a breeding hair agent about a blending ratio demonstrated to the maximum, a case where the ingredient (B) / ingredient (A) is 1 / 100000 - 500/1 in a weight ratio was preferred, and an outstanding effect made into the purpose of this invention was accepted.

[0011]It is preferred to use together at least one sort of compounds chosen from a group which consists of fatty acid and alcohol which have the chain length of (C) odd number, and those derivatives further in this invention in addition to the above (A) and the (B) ingredient. If the number of carbon atoms which constitute a chain is odd things, even if fatty acid which has the odd chain length which uses as a compound of an ingredient (C) here, and fatty acid of those derivation inside of the body are saturated fatty acid and they are unsaturated fatty acid, they will not be cared about. Unsaturated fatty acid may include more than double bonds of two or more. It may be sufficient higher fatty acid [like pentadecanoic acid (chain length 15) or heptadecanoic acid (chain length 17)] whose propionic acid (chain length 3) and lower fatty acid like a valeric acid (chain length 5) are also. among these, the carbon numbers 3-25 -- a thing of 9-19 is more preferably good. Any derivative of such odd number chain length's fatty acid can be used for a breeding hair agent of this invention. However, it cannot be overemphasized that what has an adverse effect on a human body cannot be used. The following are raised as an example of a desirable derivative.

b) Following general formula [I]or[II] Monoglyceride shown, [0012]

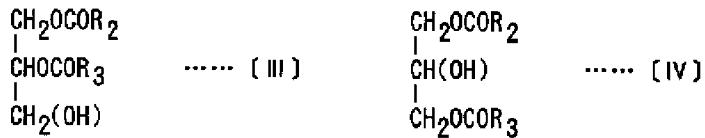
[Formula 2]



[0013](However, R₁ expresses the straight-chain-shape organic group which has even chain length)

**) following general formula [III] -- or [IV] the jig resaler to whom it is shown -- ide, [0014]

[Formula 3]



[0015](However, R_2 and R_3 are chain organic groups, and at least one side expresses the straight-chain-shape organic group which has even chain length among these)

**) Following general formula [V] Triglyceride shown, [0016]

[Formula 4]



[0017](However, R_2 , R_3 , and R_4 are chain organic groups, and at least one expresses the straight-chain-shape organic group which has even chain length among these)

**) Following general formula [VI] Fatty acid salt shown,[Formula 5] $(\text{R}_1\text{COO})_n\text{M}$ [VI]

(However, R_1 expresses the integer corresponding to [corresponding to the metal atom in the straight-chain-shape organic group and M which have even chain length] the valence of M in n)

**) Following general formula Ester shown by [VII],[Formula 6] R_1COOR_5 [VII]

(However, the straight-chain-shape organic group and R_5 in which R_1 has even chain length express univalent or dihydric alcohol residue, amine residue, polyoxyethylene residue, sorbitan residue, or sucrose residue)

[0018]** Following general formula [VIII] The 1st amide expressed,[Formula 7] $\text{R}_1\text{CONR}_6\text{R}_7$ ---
----- [VIII]

(However, the straight-chain-shape organic group in which R_1 has even chain length, R_6 , and R_7 express hydrogen or an organic group)

**) Following general formula [IX] The 2nd amide expressed, [0019]

[Formula 8]



[0020](However, the straight-chain-shape organic group and R_6 in which R_2 and R_3 are chain organic groups, and either at least has even chain length among these express hydrogen or an organic group)

**) Following general formula [X] The 3rd amide expressed, [0021]

[Formula 9]



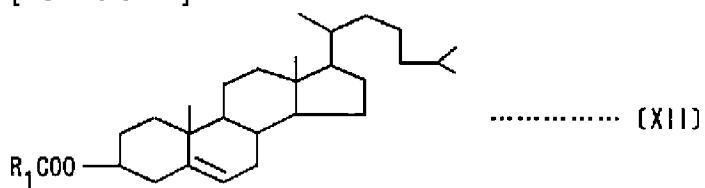
[0022](However, R_2 , R_3 , and R_4 are chain organic groups, and at least one expresses the straight-chain-shape organic group which has even chain length among these)

**) Following general formula [XI] The dibasic acid expressed and its salt[Formula 10]
 $\text{HOOCR}_8\text{COOH} \cdots \cdots \text{ (XI)}$

(However, R_8 expresses a straight-chain-shape organic group which has odd chain length)

**) Following general formula [XII] Sterol ester expressed, [0023]

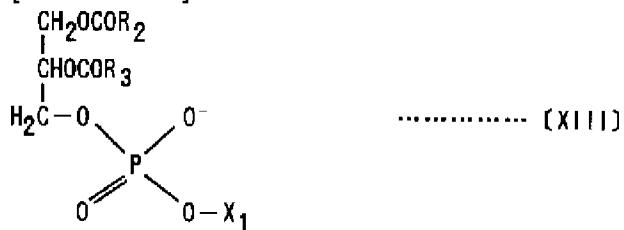
[Formula 11]



[0024](However, R_1 expresses the straight-chain-shape organic group which has even chain length)

**) Following general formula [XIII] Phospholipid shown, [0025]

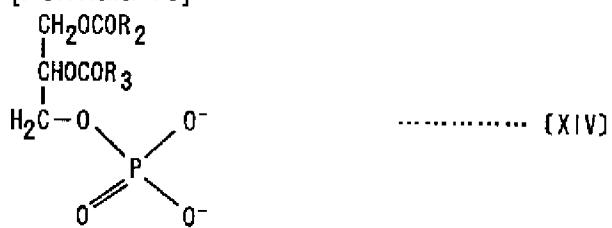
[Formula 12]



[0026](However, the straight-chain-shape organic group and X_1 in which R_2 and R_3 are chain organic groups, and either at least has even chain length among these express the Kolin residue, ethanolamine residue, serine residue, or inositol residue)

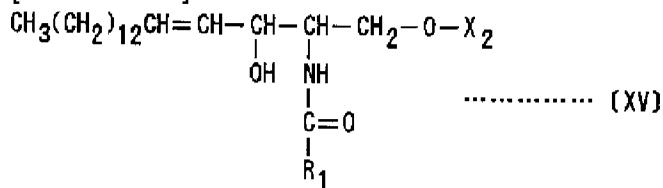
**) Following general formula [XIV] Phosphatidic acid shown, [0027]

[Formula 13]



[0028](However, R_2 and R_3 being chain organic groups, and either at least expressing the straight-chain-shape organic group which has even chain length among these), and a WA following general formula [XV] Sphingolipid shown, [0029]

[Formula 14]



[0030](However, the straight-chain-shape organic group and X_2 in which R_1 has even chain length express sugar residue, phosphate residue, or amino base residue) as the inside of the above-mentioned formula, and R_1 -- the carbon numbers 2-24 -- the thing of 8-18 is more preferably desirable. Formula [III] [IV]**[XIII]It reaches. [XIV] R_2 and R_3 which can be set are good even carbon numbers and for one either to have a carbon number of the above-mentioned even number often [it is desirable and / 2-24, and having 8-18 more preferably] and most preferably in both R_2 and R_3 at least. Formula[V]**[X] Set and it is good even carbon numbers and for all the R_2 - R_4 to have [any one of R_2 - the R_4] a carbon number of the above-mentioned even number often [it is desirable and / 2-24, and having 8-18 more preferably] and most preferably. Formula[VII]As monohydric alcohol of inner R_5 , alcohol of the carbon numbers 1-18, such as methanol and ethanol, is raised, and mono- ** JI and triethanolamine are raised as amine residue. Formula[VIII]It reaches. [IX]As inner R_6 and an organic group of R_7 , the alkyl group of the carbon numbers 1-18, such as a methyl group and an ethyl group, is preferred.

[0031]Formula[XI]as inner R_8 -- the carbon numbers 1-23, such as a methylene group, -- a hydrocarbon group of 1-17 is more preferably preferred. Formula[XIII]When inside X_1 is the Kolin residue, it becomes a phosphatidylinositol at the time of a phosphatidyl serine and inositol at the time of a phosphatidylethanolamine and serine residue at the time of phosphatidylcholine and ethanolamine residue.

[0032]Formula[VI]Sodium, potassium, lithium, etc. are raised as inner M. In this invention, one sort or two sorts or more of mixtures, I - WA, which are its derivative besides fatty acid of odd chain length can be used as a (C) ingredient. As these examples, with fatty acid, nonanoic acid, tridecanoic acid, pentadecanoic acid, Carry out and b) Tridecanoic acid monoglyceride, pentadecanoic acid monoglyceride, as heptadecanoic acid monoglyceride and RO -- an undecanoic acid jig resaler -- ide. a tridecanoic acid jig resaler -- ide and a pentadecanoic acid

jig resaler -- as ide and Ha -- nonanoic acid triglyceride. Tridecanoic acid triglyceride, pentadecanoic acid triglyceride, As diacetyl monopentadecanoate glyceride and NI, nonanoic acid potassium salt, As sodium salt pentadecanoate and HO, ethyl pentadecanoate, methyl nonadecanoate, Carry out and as pentadecanoic acid amide and TO **) N-acetylpentadecanoic acid amide, Carry out and as N,N-diacetylpentadecanoic acid amide and Li **) 1,13-tridecamethylenedicarboxylic acid, Carry out and as cholesterol pentadecanoate and RU **) A 1,2-dipentadecanoly- glycero 3-FOSURIRU choline, **) It carries out and an N-pentadecanoly sphingosine 1-phosphorylethanolamine is raised as 1,2-dipentadecanoly-glycero 3-phosphoric acid and WA.

[0033]If the number of carbon atoms which constitute a chain is odd things, even if alcohol which has the chain length of odd number which can be used as a (C) ingredient of this invention, and alcohol of those derivation inside of the body are saturated alcohol and they are unsaturated alcohol, they will not be cared about. Unsaturated alcohol may include two or more double bonds. It may be sufficient higher alcohol [like tricosyl alcohol (chain length 23) or pentacosyl alcohol (chain length 25)] whose lower alcohol like propyl alcohol (chain length 3) or amyl alcohol (chain length 5) is also. A hydroxyl group may be combined with any carbon atom. It is [among these] good the carbon numbers 3-25 and to use a thing of 9-19 more preferably. In this invention, a derivative of the above-mentioned alcohol can also be further used as an ingredient (C). A typical derivative is esterification material and an etherification thing of odd number chain length alcohol. Esterification material is expressed with a following general formula.

[0034]

[Formula 15] R_9-O-R_{10} [0035]the inside of a formula, and R_9 -- odd number chain length alcohol residue -- desirable -- the carbon numbers 3-25 -- the odd number chain alcohol residue of the carbon numbers 9-19 is shown more preferably. R_{10} -- fatty-acid-residue (what has chain length of carbon numbers 2-24 preferably): -- the residue of inorganic acid, such as residue [of organic acid like succinic acid, citrate, fumaric acid, lactic acid, pyruvic acid, malic acid, and oxaloacetic acid]; or phosphoric acid, is shown. An etherification thing includes what is expressed with a following general formula.

[0036]

[Formula 16] R_9-O-R_{11} [0037]the inside of a formula, and R_9 -- odd number chain length alcohol residue -- desirable -- the carbon numbers 3-25 -- the odd number chain alcohol residue of 9-19 is shown more preferably. R_{11} -- monohydric alcohol residue (what has chain length of carbon numbers 2-24 preferably); -- glycerin. The residue of sugar like residue [of polyglycerin, ethylene glycol, propylene glycol, and polyhydric alcohol like butanediol]; or grape sugar, a ribose, galactose, arabinose, mannose, xylose, sorbitol, and mannitol is shown.

The etherification thing may contain two or more odd number chain length alcohol residue in the monad, for example like JI of glycerin, or the Tori odd number chain length's alkoxide. The indispensable thing for the odd number chain length alcohol derivative used for the breeding hair agent of this invention is only that the residue of the odd number chain length alcohol mentioned above is included. Therefore, the acid residue in above-mentioned esterification material may have various substituents, for example. Similarly, the alcohol residue and sugar residue in the above-mentioned etherification thing may also be replaced by various substituents. But it cannot be overemphasized that it must not be what has an adverse effect on a human body.

[0038]As the above-mentioned odd number chain alcohol and its derivative, specifically, Undecyl alcohol, tridecyl alcohol, pentadecyl alcohol, One sort or two sorts or more of mixtures of heptadecyl alcohol, nonyl acetate, succinic acid undecyl, citrate pentadecyl, TORIUN decyl glyceryl ether, and TORIPENTA decyl glyceryl ether can be raised. A compound of the above-mentioned ingredient (C) which is an essential ingredient of this invention can be blended by arbitrary concentration into a breeding hair agent. Usually, although based also on types of products and frequency in use, it is good in various breeding hair agents to blend 0.1 to 10% preferably about 0.01 to 20%. According to the purpose of use, arbitrary ingredients other than the above-mentioned active principle can be blended with a breeding hair agent of this invention. As such an ingredient, purified water, ethanol, polyhydric alcohol, cellulose, a surface-active agent, oil and fat, ester oil, amino acid, a keratolytic drug, polymer resin, a color material, and an ultraviolet ray absorbent besides perfume can be mentioned, for example.

[0039]As polyhydric alcohol, glycerin, a 1,3-butylene glycol, A polyethylene glycol, sorbitol, propylene glycol, and pentaerythritol as cellulose, Hydroxymethylcellulose, hydroxypropylcellulose, and hydroxypropylmethylcellulose as a surface-active agent, Sorbitan fatty acid ester species (sorbitan monolaurate, sorbitan mono- olate, etc.), TORIISO stearate etc. polyoxyethylene hydrogenated castor oil and polyoxyethylene hydrogenated-castor-oil mono- **** as oil and fat, polyhydric alcohol fatty acid ester (tri-2-ethylhexanoic acid glycerin.) Safflower oil, Oenotherae Biennis oil, jojoba oil, etc. Tori trimethylolpropane isostearic acid acid etc. as ester oil, Unsaturation aliphatic alkylester (ethyl oleate and isopropyl linolate), methyl myristate, and myristic acid isopropyl as amino acid, In methionine, serine, a glycine, cystine, etc., as a keratolytic drug, both sexes, cationicity, anionic, and nonionic polymer as polymer resin further as an ultraviolet ray absorbent, [salicylic acid, resorcinol etc.] Methoxycinnamic acid octyl (neo HERIOPAN AV), oxybenzone, urocanic acid, etc. are mentioned.

[0040]In accordance with a conventional method, breeding hair agents of this invention are gestalten, such as a homogeneous solution, a lotion, and JIERU, and can be used as external preparations, an oral administration agent, etc. Can take a breeding hair agent of this invention

and a gestalt of an aerosol composition in that case, In addition to the above-mentioned ingredient, compressed gas, such as combustible gas; nitrogen gas, such as lower alcohol; butane, such as n-propyl alcohol or isopropyl alcohol, propane, isobutane, liquefied petroleum gas, and wood ether, oxygen gas, carbon dioxide, and nitrous oxide gas, can be contained. [Effect of the Invention] The breeding hair agent of this invention shows the outstanding hair growth promotion operation. Although an example is given to below and this invention is explained to it, this invention is not limited to these examples.

[0041]

[Example]

One ingredient of examples (A), the ingredient (B), and the ingredient (C) were dissolved in ethanol 95%, the breeding hair agent sample was prepared, and the following examining method estimated the hair restoration effect. A result is shown in table-1. The result about a comparative example is shown in table-2. Some which were extracted from the pulp of *Elaeis guineensis* of the *Elaeis guineensis* group, and were refined are in front with palm oil tocotrienol, and the weight ratio of alpha-tocotrienol:gamma-tocotrienol:delta-tocotrienol of what was used here is a thing of 26:58:16. The quantity in front is weight %.

[The hair restoration effect examining method] The regions of back of the C3 H/Heslc mouse in the resting phase of a hair cycle were depilated with hair clipper and a shaver, and the experiment was presented as one groups [ten]. Every 0.1 ml each of test samples were applied back which was depilated once per day. The trichogenous effect of each test sample measured the hair-growing area of mouse depilation regions of back, and measured it with the ratio to the depilated area. The days which the rate of 50% hair growing by each test sample takes were counted, and the days which reach the rate of hair growing 50% indicated in front the days shortened compared with the case where only ethanol is applied as "promotion days."

[0042]

[Table 1] Table -One (this invention)

No 1 2 3 4 5 6d1-alpha-tocotrienol 0.5 0.5 0.5 Palm oil tocotrienol 0.5 0.5 0.5 Forskolin 0.05 0.05 0.05 KOREUSU root extract 2.0 2.0 2.0 (forskolin 2.1% content)

Monoglyceride pentadecanoate 0.1 succinic-acid undecyl 0.5 [Hair restoration effect]

Promotion days 8 8 10 10 11 12[0043]

[Table 2] Table -Two (comparative example)

No. 1* 2* 3* 4* 5* 6*d1-alpha-tocotrienol 0.5 0.4 d1-beta-tocotrienol 0.5 0.1 d1-gamma tocotrienol 0.5 0.1 d1-delta-tocotrienol .0.5 0.1 palm-oil tocotrienol 0.595% ethanol *** *** *** ***

**[Hair restoration effect]

Promotion days 5 5 5 6 7 7[0044]

[Table 3] Table -Two (continuing : comparative example)

No. 7* 8* 9* 10* forskolin 0.05 KOREUSU root extract 2.0 (forskolin 2.1% content)

Monoglyceride pentadecanoate 0.1 succinic-acid undecyl 0.5[Hair restoration effect]

Promotion days 5 5 7 7[0045]The result of table-1 shows that a synergistic effect will be clearly accepted about hair growth promoting actions if an ingredient (A) and an ingredient (B) are used together, and the hair growth promoting actions which were further excellent when the ingredient (C) was further used together are obtained.

The breeding hair agent of the presentation shown for ranking second example 2 was prepared.

monoglyceride pentadecanoate 3.0 weight %14,15-dihydroforskolin 1.0 sorbitan monolaurate 4.0 glycerin 0.5 safflower oil 0.2 palm-oil tocotrienol 0.2 items: -- alpha-tocotrienol: -- 25%. beta-tocotrienol: -- 25% gamma-tocotrienol: -- 40% delta-tocotrienol: -- 10% Yuka Former 205S (made by Mitsubishi Petrochemical Co., Ltd.) 0.1 perfume 0.3 99.5% ethanol The remainder Total 100.0 %

[Translation done.]